REMARKS

The rejections have been considered at length. However, for the reasons set forth below it is submitted that the claimed subject matter would not have been rendered obvious by the cited references.

Claims 1, 3-7, 9, 11-14, 18-39 are pending and have been examined on the merits. Claims 1, 3-7, 9, 11-14, 18-22, 24-29 and 31-39 have been amended hereinabove. No new matter has been added.

In the Final Office Action, the claims have been rejected as follows:

1. Claims 1, 3-7, 9-11-13 18-29 and 30-39 stand rejected under 35 U.S.C. § 103(a) as being obvious over Goldenberg (U.S. Patent Application Publication No. 2001/0006618, hereinafter "Goldenberg") in view of Cokgor et al. (Journal of Clinical Oncology, 2000, Vol. 18, pages 3862-3872, hereinafter "Cokgor); and
2. Claims 1, 3-7, 11-14, 18-29 and 30-39 stand rejected as being obvious over Goldenberg in view of Cokgor and MacPhee et al. (U.S. Patent No. 6,054,122, hereinafter "MacPhee").

Applicants respectfully traverse. As initial matter, the claims have been amended solely to be in better condition for allowance. Therefore, entry of the claim amendment is respectfully requested.

Applicants wish to incorporate by references the previously filed response. In addition, Applicants provide the following additional comments.

The presently claimed invention is directed to a method of treating a patient with solid tumor by first administering intraoperatively a first agent as avidin, streptavidin, etc and then administering postoperatively a second anticancer agent having affinity for the first agent (*e.g.*,

page 8, lines 12-15 and lines 17-24). Because avidin in endowed with tumor tropism, the presently claimed invention can be successfully used on tumors which do not express antigens (*e.g.*, page 8).

Goldenberg does not disclose Applicant's invention. Goldenberg only provides for a method for injecting a patient with a first composition comprising either streptavidin- or avidin-conjugated antibody, biotinylated antibody to be used in conjunction with avidin and biotin…wherein the antibody is an antibody or an antibody fragment which specifically binds a marker produced by or associated with the lesion (*e.g.*, page 1, paragraph [0003], page 3 paragraph [0036]). Further, Goldenberg is completely silent with regard of using streptavidin, avidin etc only, instead of a tumor specific antibody. However, unlike in Goldberg, the first composition of Applicants' invention does not contain a monoclonal antibody and the affinity for the tumor is provided by avidin only.

Accordingly, there is no suggestion or motivation in Goldenberg for using a first agent selected from the group consisting of avidin, streptavidin, their polymeric derivatives and their derivatives with polyethylene glycol followed by a second anticancer agent. On the contrary, Goldenberg teaches away from the presently claimed invention in that it specifically "conjugates" the streptavidin or the avidin with tumor-specific antibodies.

Accordingly, Goldenberg does not disclose Applicants' invention and would not have rendered obvious the claimed subject matter to one skilled in the art.

In addition, Applicants respectfully assert that the Examiner's comment on page 4 of the Final Office Action related to inherency is improper and wrong.

A claim is considered invalid, if a single reference inherently, discloses every limitation of the claim at issue. Inherency is predicated on the fact that anticipation cannot be avoided

merely because an element is undisclosed and unrecognized in the reference, but is a "deliberate or necessary consequence" of the reference disclosure. "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer". *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

Further, there is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure *at the time of the invention*, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003). However, these are not the facts of this case.

As set forth above, inherency is a "deliberate or necessary consequence of the reference disclosure". In this specific case, inherency is not a deliberate or necessary consequence of Goldenberg's disclosure. In paragraph [0036], Goldenberg clearly discloses a composition of avidin-conjugated antibody, streptavidin-conjugated antibody etc. The presently claimed invention, on the other hand, does not disclose a composition, but simply avidin, streptavidin etc, without any antibody. Nowhere Goldenberg teaches the possibility to use avidin, streptavidin etc by themselves. In fact it specifically teaches that "the antibody is an antibody or antibody fragment which specifically binds a marker produced by or associated with the lesion." Therefore, for these additional reasons, it is respectfully submitted that Goldenberg would not have rendered obvious the claimed subject matter.

Cokgor does not provide for the missing links in that it suffers from the same defects. Cokgor also discloses the administration of I-131 labeled antibody administered into surgically created resection cavities in patients suffering from malignant gliomas (*e.g.*, the abstract). As such, the combination of Goldenberg with Cokgor still is not the presently claimed invention.

Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so. *In re Kahn*, 441, F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006). As set forth above, the teaching of Goldenberg cannot be modified and combined with the teaching of Cokgor to produce the claimed invention. Accordingly there cannot be any motivation in the teaching of the prior art to modify and combine the teaching of Goldenberg with the teaching of Cokgor. On the contrary, Applicants respectfully submit that the Examiner's conclusion that two references can be modified and combined as presently claimed is based on improper hindsight. *W.L Gore & Associates, Inc. v Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1954).

Accordingly, for all of these reasons, Applicants submit that the subject matter of claims 1, 3-7, 9, 11-13, 18-29 and 30-39 would not have been rendered obvious by the combination of the cited references and withdrawal of the rejection of the claims under 35 C.F.R. § 103(a) is respectfully requested.

MacPhee does add anything to the combination of Goldenberg with Cokgor. MacPhee only discloses a fribin sealant dressing which could be supplemented with a number of drugs to prevent infections, inflammations etc (*e.g.*, the abstract).

Therefore, one of ordinary skill in the art would not have received any guidance from MacPhee to administer a first agent selected from the group consisting of only avidin, streptavidin etc

Accordingly, Applicants assert that the combination of Goldenberg in view of Cokgor and MacPhee also fails to render obvious the claimed subject matter to one skilled in the art. Thus, withdrawal of the rejection of the claims under 35 C.F.R. § 103(a) is respectfully

requested.

This response is being filed within shortened statutory period for response. Thus, no further fees are believed to be required. If, on the other hand, it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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